Appln No.: 09/824,587
Amendment Dated: June 21, 2004
Reply to Office Action of March 19, 2004

REMARKS/ARGUMENTS

This is in response to the Office Action mailed March 19, 2004 for the above-captioned application. Reconsideration and further examination are respectfully requested.

Applicants note that the previous rejections have been withdrawn.

Claims 21-50 stand rejected as indefinite under 35 USC § 112, second paragraph. Applicants have made some clerical amendments to improve readability of claim 21, but otherwise respectfully traverse this rejection.

The Examiner states that the "claim appears to be drawn to a method for differentiating between two different states of an analyte that exists in a plurality of different forms, i.e., a method for detecting different isoforms of an analyte." Applicants respectfully submit that this statement is not precisely correct. Applicants' invention relates to the differentiation between two or more "states" which are each characterized by the presence of an analyte in different forms (for example isoforms). The nature of the difference may be one of kind. that is that in state one, form one is present, and in state two, form two is present. More commonly, however, the difference is one of degree. That is, in state one, form one is 50 percent and form two is 50%, while in state two form one is 75% and form two is 25% (These number are arbitrary examples only). Both of these circumstances are described by the language in the claim, i.e., that the different states contain different forms of the analyte in different relative amounts, since all of one form and non of the other is still a relative amount.

The Examiner also states that "it is unclear if applicant is claiming a method for differentiating between at least two different isoforms of an analyte, of if two different states of an analyte are differentiating by detecting the amount of the same analyte at different time intervals in different samples." This statement is in part responded to in the comment above. However, the Examiner's comments about detecting the amount of sample at different time intervals is not understood. The actual required steps of the method are as set forth in the claim.

The first step is obtaining first and second assay samples containing the analyte. The samples are either aliquots of a single sample or contemporaneous samples from the same source. This means that the samples are reasonably expected to be the same, but that the method ology of collection is not relevant.

The two assay samples are treated differently in accordance with the method of the invention, but the difference does not different time intervals in the sense of duration of the assay. Rather, the first specific binding assay is a stepwise assay, in which the first assay sample is reacted with a first binding agent to form a first binding agent/analyte complex, which is then subsequently reacting the first binding agent/analyte complex with a second binding agent to

form a first binding agent/analyte/second binding agent complex. The second second specific binding assay is a non-stepwise assay in which the second assay sample is reacted **substantially simultaneously** with the first binding agent and the second binding agent to form a first binding agent/analyte/second binding agent complex.

The assays each produce a result indicative of the amount of first binding agent/analyte/second binding agent complex formed. Because at least one of the first and second binding agents used in the method of the invention has a different specificity for the forms of the analyte, the amount of complex formed using these two methods can be different, depending on the relative amounts of the forms of the analyte. As a result, these two assays allow differentiation between different states of the analyte.

The Examiner also stated that claim 21 is confusing because "there is no clear correlation between the preamble of the claim and what is being detected." Applicants have amended claim 21 to repeat the language of the preamble at the end of the claim.

In view of the foregoing remarks, Applicants submit that the rejection under 35 USC § 112, second paragraph has been overcome. Withdrawal of this rejection is respectfully urged.

The Examiner rejected claims 48-50 under 35 USC § 112, first paragraph, as lacking enablement. These claims recite specific hybridoma cell lines, and the basis for the rejection is an assertion that "the specification lacks complete deposit information for the hybridoma cell lines known as ECACC 00032004 and ECACC 00032005." Applicants attach a copy of the deposit terms of the ECACC for patent deposits. As reflected in these terms, all deposits to the ECACC are made under the terms of the Budapest Treaty. Accordingly, the rejection should be withdrawn.

The Examiner also rejected claims 21-50 under 35 USC § 112, first paragraph, as lacking enablement. Essentially, the Examiner asks the question, if the reagents are same in the two assay, and the samples are the same, how can anything be differentiated. Specifically, she asks "because only the end result is observed (i.e., the labeling effect of the second binding reagent), how does one detect whether is is isoform A or isoform B, for example, that is bound by the binding reagent. The short answer to this is, as explained above, that the reagents are used differently in the two assay: one assay is stepwise, and the other is substantially simultaneous.

Example 3 provides an illustration of how this works. In the two step assay, the sample or standard is applied to the coated wells, and allowed to incubate for a period of time (in the example 6 hours). Unbound material for the sample is then washed away, and labeled second binding reagent is added and incubated for one hour. In the one step assay, both the sample and the labeled second binding reagent are added to the coated wells at the same time. As the results

on Page 18 show, although the reagents are the same, and the samples are the same, the amount of reagent captured in the two assay methodologies is quite different.

The test results on page 18 are reported as a ratio, but it is noted that this is merely a compact form of expressing comparison without dealing with absolute values of readings which can depend on the radioactivity of the label or the kind of the label, the quality of the measuring equipment, and the absolute concentration of analyte in the sample. It is noted, however, that qualitative comparisons may also be used (for example darker vs lighter, Page 10, line 31-Page 11, line 4).

The Examiner also states that there is no "teaching that the different isoforms of the analyte can be differentiated using the method of the invention." Applicants respectfully point out that what Applicants claim is not differentiating isoforms, but differentiating analyte "states" which may be the result of compositions having the same isoforms in differing relative amounts. This is exactly what is shown in Example 3.

The Examiner also focuses on the passage on Page 11, lines 5-19 which relates to determinations of transitions from a pre-menopausal to post-menopausal state and the fact that these tests may be performed as a series of tests. It is not clear what the Examiner's concern is with this passage. At each stage in this series of tests, both the first and second assay are performed on contemporaneous samples. Furthermore, this is a specific description of an assay procedure for more accurate diagnosis, not a critical or limiting condition.

In view of the foregoing, Applicants submit that the rejection for lack of enablement should be withdrawn. If the rejection is to be maintained, however, Applicants request an interview to discuss the basis for the Examiner's concerns so that clarification can be provided.

For these reasons, this application is now considered to be in condition for allowance and such action is earnestly solicited.

Respectfully Submitted,

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